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Tracy M. Sonneborn - An Appreciation

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Two roads diverged in a wood, and I --
I took the one less traveled by,
And that has made all the difference.
--Robert Frost

The papers in this volume of Genetical Research are submitted by his students and associates in tribute to Professor Tracy M. Sonneborn on the occasion of his seventieth birthday. For nearly forty years, Sonneborn has trained most of the investigators in ciliate genetics, nearly three dozen as doctoral students, nearly two dozen as postdoctorals, and indirectly, ever rising numbers of scientific grandchildren. He remains the unchallenged master, the chief repository of wisdom, a steady source of inspiration and challenge.

Ciliate genetics, at least in its modern phase, is largely a Sonneborn construction but it was not built in a vacuum. Sonneborn was one of the doctoral students (1928, Johns Hopkins) of Herbert Spencer Jennings, and he elaborated many of Jennings' values and interests. Unlike some other students of the protozoa, Jennings refused to consider protozoa as creatures apart from other life forms, but sought through their particularities to discover principles of general application; in this sense he was a biologist rather than a protozoologist. Most of Jennings' later studies were limited to the protozoa, but they ranged from pioneer explorations in cellular behavior and clonal aging to the beginnings of population genetic analysis. Sonneborn likewise refused to be limited to one level of life's hierarchy or to one narrow discipline. He resembled his mentor also in certain personal characteristics. Notable in both men is a penchant for careful, systematic, even painstaking analysis.

But Jennings' experimental work was hampered by his inability to control mating in his protozoa, and Sonneborn's first major contribution to the field came in 1937 when his discovery of mating types in Parmecium aurelia overcame that barrier. The exploitation of controlled mating led quickly to several fundamental discoveries. He found that Paramecium aurelia (and indeed most ciliate "species") is a species complex composed of many well-defined and effectively isolated gene pools. It is an interesting historical aside

that Sonneborn's discoveries permitted a new and important chapter in Jennings' own research career that continued until his death.

The "biological species" of the ciliates were first named "varieties," later "syngens," and some have finally achieved full legitimization as taxonomic species. In spite of their apparent similarities, these sibling species sometimes show large differences in important biological attributes. Sonneborn's comparative studies of these ciliate life histories led him into one of his most seminal but still ill-appreciated explorations -- into the poorly defined area of breeding economies. In a careful analysis of the special adaptations of the ciliates, he showed that most of their hitherto unexplained peculiarities were related to a single central issue: "Who mates with whom." The ciliates provide an otherwise unexampled array of very similar organisms living in very similar habitats but ranging from obligate inbreeders to compulsive maters with strangers. The ecological and evolutionary genetic of the ciliates are only in their beginnings, but we must expect interesting developments from these organisms which have for so long accumulated molecular variation while being constrained in narrow ecological niches. The ciliates may provide unparalleled materials for the study of evolutionary strategies.

One of the studies for which Sonneborn is best known is that dealing with kappa, the "killer" cytoplasmic factor. These cytoplasmic elements were for several years the best understood of the "plasmagenes." They were considered important at first because they provided a possible resolution to the developmental riddle: the "hereditary" differences in cell lineages with identical nuclei. The significance of plasmagenes in developmental differentiation diminished with better understanding of nuclear capabilities, and also with the recognition that kappa particles were bacteria rather than some simple gene-like entity. Later, however, the kappa work provided a model for the study of other cytoplasmic elements, such as chloroplasts and mitochondria, which are more general protoplasmic structures. The kappa work also led to theoretical confrontations around the issues of native and foreign cellular constituents, of normal and infectious genetic elements. These considerations foreshadowed the discovery of episomes, and they reverberate

still in our search for the origins of organelles and the mechanisms of cancer. In more recent years kappa has been studied by one of Sonneborn's students (and several grand-students) as an interesting thing in its own right, as a component in an exceedingly intimate symbiosis. It continues to provide surprises as new interactions are exposed.

Another trait simultaneously studied by Sonneborn and his associates seemed initially to be very similar to the killer character. Differences in immobilizing antigens of Paramecium behave in some crosses in precisely the same way as do differences between killers and sensitives; with cytoplasmic mixing, exconjugants become alike; without cytoplasmic mixing exconjugants remain different. Yet the Sonneborn group showed that the specificities being regulated were encoded by nuclear and not by cytoplasmic genes. Sonneborn was one of the first to recognize that "cytoplasmic inheritance" is not a phenomenon, but phenomena, with a diversity of mechanisms. Cytoplasmic inheritance need not imply "self-reproducing" cytoplasmic elements. Some detailed mechanisms for the perpetuation of differences in "nucleocytoplasmic states" have been discovered in procaryotes, but the first clear demonstration of the phenomenon was provided in a eucaryote. Perhaps the first detailed understanding of a mechanism for maintaining such states of gene action in a eucaryote will yet come from the ciliates, as current studies in the chemistry, genetics and physiology of serotypes move forward.

Other studies concerned with the perpetuation of cellular differences date from the same early period and continue to the present. Sonneborn showed that mating types in many ciliates are epigenetically determined. Through a series of clever and meticulous experiments he demonstrated that mating type determination is achieved by a specific alteration in the nucleus during a critical time in its development. The capabilities of the nucleus are restricted by its genotype; its development is influenced by the environment and, in some cases, by the cytoplasmic surroundings. In the later case an example of "cytoplasmic inheritance" was exposed as a cryptic case of nuclear differentiation. When these experiments were first reported their general significance was questioned, because the notion of nuclear regulation was not yet popular. Mating type inheritance in ciliates

still provides one of the clearest examples of nuclear differentiation, and recent successes in some ciliates in defining the chemistry of the mating substances offer encouragement that we may soon understand the mechanisms.

In recent years Sonneborn has devoted considerable efforts to an understanding of the ciliate cortex and to its role in morphogenesis. These studies once again challenge some commonly accepted verities. They demonstrate structural inertia in growing systems, whereby differences in organization of cellular elements tend to maintain themselves indefinitely - even when supplied with the same raw materials and grown in the same environments. The role of pre-existing structure (cytotaxis) in guiding new structures is abundantly documented in ciliates and is certainly of some significance in all living systems.

This brief survey does poor justice to the diversity and depth of Sonneborn's experimental work. He also studied clonal aging in ciliates and followed these interests with explorations into human aging. He has conducted over a long period of time an heroic campaign to induce and identify genetic markers for all the 40-plus chromosomes of P. aurelia. He has carried out comparative studies on all the genetic species and has brought under cultivation still other protozoans.

In addition to all this, Sonneborn has been a major motive force in several areas of ciliate biology in which he has never associated his name directly. Unlike the practice in many other traditions, Sonneborn would only accept coauthorship for work in which he made a substantial observational or experimental contribution. Thus, most of his doctoral students and post-doctoral associates published their research alone, though only we can know the countless hours of discussion and writing he invested in each of us, and the rarity of the sentence that passed his scrutiny without modification. Primary scientific contributions were sometimes transmitted through his formal classes (in which he reached far beyond the protozoa) or through his perenially stimulating weekly seminars (in which our analytic powers were challenged to their limits) or through his one-on-one editorial interactions (through which we learned, if ever we could, the meaning of pre-

cision). Many of the foundation stones on which his students built were given ready-cut, and never adequately acknowledged.

His protean efforts make final evaluation and summary very difficult. In preparation for this essay, I wrote to some of his former students asking guidance on this point. Specifically I asked for what contribution Sonneborn should best be remembered in 2075. Nearly all the respondents identified Sonneborn's preeminent role in promoting the use of ciliates in experimental biology. When individual accomplishments were mentioned, however, they ranged very widely, from his discovery of mating types, through his studies on cytoplasmic inheritance, to his recognition of significant roles for cellular fabrics in cellular morphogenesis. Although numerous contributions of great diversity were recalled, no single biological principle or grand generalization surfaced. Indeed several respondents remarked that it is too early to give a final judgment on the significance of Sonneborn's contributions, not merely because his work continues through his own efforts, but because his work continues also through the work of others. As one respondent notes, when the work he initiated on clonal aging continues to an understanding of its mechanism, and when his work on circadian rhythms is resolved in an understanding of cellular oscillations, and when his comprehensive interactional approach to cellular morphogenesis yields a more realistic understanding of cellular organization, <u>then</u> we will be able to evaluate what he should best be remembered for. To a greater extent than with most investigators, Sonneborn's contributions are seed in the ground. We cannot yet know which are most likely to flourish and flower.

Lest one misjudge this issue, it should be noted that this situation derives from a deliberate policy and a personal philosophy of research. Sonneborn has said on several occasions that he would not do an experiment if he thought it likely that someone else would do it. He is not challenged by the race course but by the far horizon. Given a choice of roads, he takes the one less traveled by. He is an explorer, interested in making new beginnings, rather than an exploiter willing to mine a rich vein. The result is a corpus of contributions, incomplete in important respects and difficult of final evalua-

tion but certain of a long half-life.

Although one may argue which of his scientific efforts are most weighty, agreement is easily reached about his personal characteristics. I asked my sample of Sonneborn associates to identify "the chief personal characteristic which has affected your relations with him and/or science." Although the responses came back with many diverse turns of phrase, the consensus was unequivocal. Above all else, Tracy Sonneborn is a master teacher, one who has accepted with high seriousness the master teacher's double duty to respect the truth and to respect the recipient of that truth.

At a time when undergraduate instruction was often considered a burden and a hindrance, and when his "star" status could have given him exemption, Sonneborn cheerfully carried far more than his required teaching load, and he carried it with ever renewed enthusiasm. Although he taught the beginning genetics course for many years at Indiana, it was always a new course, with new organization, new text books, new subject matter and new ways to communicate. The preparation of a lecture was always a serious business worthy of hours of intense and patient preparation, even though, or perhaps thereby, the delivery of the lecture was a dramatic and exciting happening. He could never accept from himself less than his very best efforts, and that fact conditioned mightily his students' response to his teaching.

The time Sonneborn spent in preparation is difficult to appreciate for one who did not experience him. His advanced course in microbial genetics usually focused on one particular organism. He was never content to read the current literature about that organism and to deal with recent reviews. He read, analyzed and annotated every significant paper in the history of the subject. By this means he communicated to his students his deep concern for the literal truth and an almost rabbinical respect for the written word which could not have been sustained by a casual treatment of his sources. He proved his belief in the importance of his material by the time he invested in its analysis. I once asked him how he could afford to spend so much time on his teaching. He answered that it wasn't difficult. He owed the university a 40-hour week for his teaching and housekeeping

efforts. So long as his second 40 hours were free for his own research activities, he had no reason to complain. He not only did not complain, but he actively sought involvement in teaching activities. Even near the end of his formal teaching career, he requested and taught with enormous success a large scale popular course in the meaning of biology for non-science students.

Sonneborn's teaching has never been limited to the classroom; indeed for his graduate students and associates that manifestation was sometimes neglected, until our own involvement in the classroom brought a delayed appreciation and understanding of his accomplishments there. His involvement with his research students is intense and personal, selfless and life-long. He takes every observation of nature as a serious and important event. He is excited by the unknown and the unexpected. He insists on an accuracy of observation, a rigor of design, and a perfection of expression which demands all a student is capable of. He can insist on high standards of performance and sometimes can achieve them because those standards are exemplified in his own work.

Sonneborn's magisterial relationships are not limited to a definite period and fixed place. Most of his students never leave his tutelage entirely, and many investigators the world over have had the benefit of his careful and thoughtful attention. Commenting on Sonneborn's many hours of selfless analysis and rewriting of manuscripts, one foreign respondent comments that "His efforts always touched us to our heart." If someone else is willing to spend that much valuable time and thought on our work, it and we cannot be entirely lacking in importance. Sonneborn's chief gift to his students is precisely this, a constantly renewed sense of high personal worth and human dignity, a sense of sharing in an important human endeavor.

One cannot evaluate Tracy Sonneborn without acknowledging that he is only a part of a remarkable team. Sonneborn was able to devote extraordinary hours to his professional work because his personal life was flexible and as untroubled as a mortal can hope for. He was able to extend sympathy and understanding to his colleagues and students because of the security of his own domestic situation. We cannot honor Tracy without also

honoring Ruth, and thanking her for sustaining his career and enriching all our lives.

Tracy Sonneborn has had a fair share of high honors. He is a member of the National Academy of Science, the American Philosophical Society and the American Academy of Arts and Sciences. He has served as president of the American Society of Naturalists, the Genetics Society of America, the American Society of Zoologists and the American Institute of Biological Sciences. He is a Foreign Member of the Royal Society of London and of the French Society of Protozoologists. He has received the Newcomb Research Award of the AAAS and the Kimber Genetics Award of the National Academy of Sciences. He has received coveted teaching awards at Indiana University where he has spent most of his professional career, and he was awarded honorary D. Sc. degrees from Johns Hopkins University, his alma mater, and from Northwestern University, and the University of Geneva. Our purpose on this occasion is again to acknowledge achievement and to do honor by presenting samples of that work in which Sonneborn has made so profound an investment. Above all we want to express our gratitude for having touched one who is, as one respondent notes, "simply the most remarkable human being I've ever known."

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